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(54) Title: NOVEL THERMOPLASTIC HYDROGEL POLYMER COMPOSITIONS FOR USE IN PRODUCING CONTACT LENSES AND METHODS OF PRODUCING SAID COMPOSITIONS

(57) Abstract: The present invention relates generally to production of thermoplastic materials which swell in water to produce hydrogels. These materials will hereafter be referred to as "thermoplastic hydrogels". They are useful as contact lenses or for use in vision correction prosthetics or as cosmetic devices. In particular, the invention relates to thermoplastic hydrogels which show improved flow characteristics.

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1 Novel Thermoplastic Hydrogel Polymer Compositions for use
2 in producing contact lenses and Methods of Producing said
3 Compositions

4
5 The present invention relates generally to production of
6 thermoplastic materials which swell in water to produce
7 hydrogels. These materials will hereafter be referred to
8 as "thermoplastic hydrogels". They are useful as contact
9 lenses or for use in vision correction prosthetics or as
10 cosmetic devices. In particular, the invention relates
11 to thermoplastic hydrogels which show improved flow
12 characteristics.

13
14 It is already known in the art to make contact lenses
15 using hydrogels. Generally these hydrogels do not
16 utilise poly(ethylene glycols) but are made from the
17 polymerisation of the single monomers HEMA, NVP or of
18 other products of free radical polymerisation. However,
19 these compositions generally are cross-linked and do not
20 flow and can only be moulded by reaction injection
21 moulding (RIM) or related "polymerisation in place"
22 processes, which are slow and relatively expensive

1 processes which are not particularly suited to contact
2 lens manufacture.

3

4 Attempts have been reported (US Patent number 4,644,033)
5 to incorporate the highly desirable properties of
6 poly(ethylene oxide) molecular chains into crosslinked
7 polyurethane materials for use, inter alia, in contact
8 lenses. It was found that such preparation procedures in
9 the absence of solvent produced only opaque products when
10 swollen in water. Such opaque products cannot be used
11 for the manufacture of contact lenses which demand
12 clarity. It was found that clear urethane cross-linked
13 polyethylene glycol products could be produced in the
14 presence of dry organic solvent. This adds the necessity
15 of solvent removal and raises questions of residual
16 solvent toxicity to the cost of manufacture.

17

18 Also, existing reaction injection moulding techniques
19 utilise free radical initiation or irradiation cure that
20 produces radicals. These radicals initiate a
21 peroxidation chain process, which leads ultimately to
22 damage of PEO based polymers in storage for use which
23 gives a short life to contact lenses produced from them.
24 There are also problems with bio-compatibility of
25 reaction injection moulded hydrogels which again is not
26 ideal for the manufacture of contact lenses where bio-
27 compatibility is importantant.

28

29 Additionally, the current cross linked polymer hydrogels
30 often have a very poor resistance to crack initiation and
31 crack propagation which again can be problematic when
32 producing contact lenses.

33

1 It can therefore be seen that it would be beneficial to
2 provide thermoplastic hydrogels which are capable of
3 being generally moulded under pressure so that contact
4 lenses can be easily and cheaply produced.

5

6 It is an aim of the present invention to provide a
7 thermoplastic hydrogel composition which has the ability
8 to flow under moderate shear at particular temperatures
9 below the polymer decomposition temperature.

10

11 It is a further object of the present invention to
12 provide a thermoplastic hydrogel composition which can be
13 injection or compression moulded.

14

15 It is a further object of the present invention to
16 provide a solvent soluble composition.

17

18 Another object of the present invention is to provide a
19 thermoplastic hydrogel composition which is highly bio
20 compatible.

21

22 A yet further object of the present invention is to
23 provide thermoplastic hydrogels which have a high level
24 of water swelling properties after moulding and swelling
25 with water.

26

27 It is a further object of the present invention to
28 provide thermoplastic hydrogels which can cover a range
29 of degrees of water swelling.

30

31 It is a yet further object of the present invention to
32 provide thermoplastic hydrogels that by design and choice
33 are either clear or opaque to visible light.

1

2 According to a first aspect of the present invention,
3 there is provided a method of producing thermoplastic
4 hydrogels for use in producing contact lenses, comprising
5 the steps of reacting one or more from the list;

6 polyethylene oxide,

7 polyol,

8 polyamine,

9 with a polyisocyanate and a polyfunctional amine or
10 polyalcohol.

11

12 Preferably the polyol is polyethylene glycol.

13

14 Preferably, the method also comprises the step of end
15 capping unreacted groups with a unit capable of producing
16 hydrogen bonding, π bonding, ionic bonding, hydrophobic
17 bonding and/or phase separation or forming a glassy or
18 crystalline phase separated domain.

19

20 Alternatively, according to a second aspect of the
21 present invention, the method also comprises the step of
22 end capping unreacted groups with a unit from a list of:

23 Mono-functional amine

24 Mono-functional isocyanate

25 Mono-functional anhydride

26 Mono-functional acid

27 A cyclic diacid anhydride

28 Mono-functional alcohol

29

30 Preferably the reaction between one or more from the list

31 polyethylene oxide

32 polyol

33 polyamine

1 and a polyisocyanate is prepared using a range of NCO:OH
2 or NCO:NH₂ ratios.

3
4 Optionally a biodegradable unit may be incorporated.

5
6 The biodegradable unit may be polycaprolactone, poly
7 (lactic acid), poly(glycolic) acid or
8 poly(hydroxybutyric)acid, amine or hydroxyl ended
9 poly(amino) acids (protein or peptide analogues).

10
11 The ratios are preferably selected such that, at complete
12 reaction, the product does not form a macrogel.

13
14 Preferably the first step reaction is prepared using a
15 range of NCO:OH or NCO:NH₂ ratios from 2:1 to 1:2.

16
17 Optionally where both OH and NH₂ groups are used within
18 the single reaction, a range of NCO:(OH+NH₂) ratios of 2:1
19 to 1:2.

20
21 Most preferably the first step reaction is prepared using
22 NCO:OH or NCO:NH₂ ratios of 2.0:1 to 1:1.8 and 1.8:1 to
23 1:1.8.

24
25 Optionally the range of ratios used may be extended by
26 the addition of monofunctional amines, alcohols or
27 cyanates.

28
29 Alternatively, a macrogel is prevented from forming by
30 stopping the reaction before completion.

31

1 Preferably, the reaction is stopped by the addition of a
2 monoamine, an amine terminated polymer, a mono-alcohol or
3 an alcohol terminated polymer.

4

5 Optionally, the monoamine, mono-alcohol, amine terminated
6 polymer or alcohol terminated polymer is added when the
7 reaction is partially complete.

8

9 Alternatively, an amine or alcohol is admixed at the
10 outset thus removing the possibility of gelation.

11

12 Preferably, the amine is added in the form of amine
13 carbonate.

14

15 Typically, products with NCO end groups are subjected to
16 a final curing by immersion in liquid water or steam
17 after moulding.

18

19 Preferably, in the second stage the unreacted groups are
20 capped with an amine.

21

22 Optionally, unreacted NCO groups are endcapped.

23

24 Another option is that unreacted OH groups are endcapped.

25

26 Preferably, terminal NCO groups are converted into a
27 strongly hydrogen bonding urea group.

28

29 Preferably, the unreacted groups are capped with an
30 aliphatic amine.

31

32 Optionally, the amine group is attached to a long linear
33 or branched alkyl group or to an aryl- or aralkyl-amine.

1
2 Optionally, the amine group is attached to polymers or
3 low molecular weight pre-polymers.
4

5 Alternatively, excess OH groups are capped with one or
6 more molecules from the list of;
7 mono-isocyanate ended aromatic molecules,
8 mono-acid anhydride ended aromatic molecules,
9 mono-isocyanate ended aliphatic molecules,
10 mono-acid anhydride ended aliphatic molecules
11 reaction product of a monoamine with a di(or higher)
12 isocyanate.
13

14 The groups used in the endcapping process allow the
15 polymers to interact with physical or chemical cross-
16 linking. The separate molecules or particles therefore
17 bind to each other.
18

19 According to the third aspect of this invention there is
20 provided a thermoplastic hydrogel for use in producing
21 contact lenses, prosthetic lenses or cosmetic lenses
22 produced by the methods of the first and second aspects.
23

24 Preferably, the hydrogel is completely polymerised under
25 the specific conditions that are being used.
26

27 Preferably, after polymerisation the hydrogel is heated.
28

29 Alternatively, after polymerisation the hydrogel is
30 immersed in water liquid or vapour.
31

1 Optionally, the end product may be pelletised, pressed,
2 extruded or heat, pressure, injection or compression
3 moulded.

4

5 Preferably, the end product incorporates an antioxidant
6 containing two or more hydroxyl groups.

7

8 The antioxidant may be internal or external.

9

10 Preferably, the antioxidant is ascorbic acid.

11

12 Alternatively, the antioxidant is 2,6-ditertiarybutyl4-
13 hydroxanisole.

14

15 Optionally the end product may develop opacity when
16 swollen in water, thereby behaving as though it a
17 contained a light scattering pigment with the appearance
18 of the sclera.

19

20 Optionally, the end product can incorporate dye(s).

21

22 Optionally the end product can incorporate pigment

23

24 Optionally the end product may be blended with a
25 water-soluble compatible solvent or plasticiser.

26

27 According to a fourth aspect of the present invention
28 there is provided a contact lens, prosthetic lens or
29 cosmetic lens produced from the hydrogel of the third
30 aspect.

31

1 An example of the present invention will now be
2 illustrated by way of example only and with reference to
3 the following figure, in which:

4

5 Figure 1 shows typical end groups that could be envisaged
6 as being associated in stacks as shown.

7

8 In the preferred embodiment, the thermoplastic materials
9 are prepared from mixtures of di (or higher) PEG polyol
10 with a di (or higher) polyisocyanate and/or a di (or
11 higher) polyamine.

12

13 First stage materials can also be made from many step-
14 growth reactions amongst which the reaction of PEG
15 polyols with polyacids with removal of reaction-produced
16 water is an option. The production of first stage
17 materials can also be guided by the art of making alkyd
18 resins in the paint industry.

19

20 If the product from the first stage reaction is made from
21 a mixture of PEG diol, 1, 2, 6-hexantriol and
22 diphenylmethane-4,4-diisocyanate, it can be prepared
23 using a range of NCO:OH ratios from, for example, 2:1 to
24 1:2. At the extremes of these ratios, the 2:1 will have
25 all NCO unreacted groups and the 1:2 ratio will have all
26 OH unreacted groups. These compositions are not able to
27 macrogel and will contain only small proportions of
28 modest molecular weight branched polymers. The product
29 is a fluid and suitable for injection, extrusion or
30 compression moulding at temperatures which are typically
31 below 150°C, although temperatures of 200°C to 250°C can
32 be utilised for short periods. It should be noted that
33 the products with NCO end groups can only be moulded and

1 subjected to final curing by immersion in liquid water or
2 steam for a suitable period.

3
4 It is possible to use intermediate NCO:OH ratios, such as
5 2:1 to 1:1.8 and 1.8:1 to 1:1.8 (and these ranges can be
6 further extended by the addition of mono-functional
7 molecules). As these still provide at complete reaction,
8 fluid systems, which when the end groups, are NCO can be
9 injection moulded and post-cured by water or steam
10 immersion. However, depending on the proportion of tri
11 or higher functional materials, ratios such as 1.6:1 to
12 1:1.6 form macrogels at as complete a reaction as is
13 possible with the NCO and OH groups present (and less
14 extended ratios are possible if mono-functional amines,
15 alcohols or cyanates are used in the first stage. The
16 resulting products are not fuseable and are not solvent
17 soluble). It is possible that the products may still be
18 used for the second stage of the process, to give useful
19 end capped products, if the reaction is stopped before it
20 has proceeded as far as possible. This operation is less
21 convenient and more difficult as the degree of completion
22 of the reaction must be determined using, for example,
23 infra-red analysis of the isocyanate absorption peak of
24 the reaction mixture, or by the viscosity of the
25 reaction. Therefore, it is much preferred to use the
26 compositions which cannot macrogel, as they can be taken
27 to completion of the first stage without fear of
28 irreversibly solidifying the reactants.

29

30 A preferred embodiment is that the first stage product is
31 a heavily branched polyurethane/PEG resin. In this
32 embodiment, the second stage is intended to convert each
33 of the terminal groups into a strongly hydrogen bonding

1 urea group. An aliphatic amine could be used and the
2 amine group could be attached to a short or long linear
3 or branched (preferably linear) alkyl group, such as
4 decyl or stearic or higher polyamines such as amine ended
5 polyethylene, or to an aryl or aralkylamine, such as
6 aniline, aminoanthracene or octylaniline. The
7 combination of the urea group and the long aliphatic
8 chain or aromatic ring will promote association and phase
9 separation of these groups with development in the
10 product material of toughness and strength by hydrogen
11 bonding and hydrophobic bonding. This will be especially
12 the case where an aromatic diisocyanate has been utilised
13 in stage one.

14
15 Figure 1 shows a diagram of a typical end group which
16 could be envisaged as associating in stacks, as shown.
17 The association of many such end groups should provide
18 increased cohesion and strength to the product.

19
20 Once the initial homogeneous mixing has been completed,
21 then the still fluid mix may be poured into suitable
22 containers, such as polypropylene moulds. The
23 polymerisation (curing) of the finished product can then
24 be completed. In order to provide an oxidation resistant
25 product, it is particularly useful to incorporate a
26 reactive antioxidant containing two or more hydroxyl
27 groups, for example, ascorbic acid (alternatively an
28 external anti-oxidants may be used). Alternatively the
29 antioxidant may be added in earlier during the first
30 stage.

31

1 The final product can be extruded or spun into film or
2 fibre or coated onto staple or continuous preformed
3 fibres to provide a form of product which can be
4 knitted, braided woven or otherwise fabricated by
5 techniques well know to those skilled in the art. The
6 product has a number of benefits, in particular as there
7 will be no unreacted extractable groups left in the
8 completed product, it is particularly useful for contact
9 lenses as it is bio-compatible. There is also the
10 benefit that materials made from the final hydrogel
11 product which are soft and strong would be comfortable
12 and re-useable again something which can be particularly
13 useful in contact lens manufacture. The final product
14 would also have the benefit of being intrinsically
15 rubbery in their dry state, and therefore contact lenses
16 would not set rigid when dried out. Also, coloured dyes
17 and pigments can be put into the final product easily,
18 which cannot be done readily with similar cross-linked
19 hydrogels and this could be useful when making "fashion"
20 contact lenses, or sun protective or prosthetic contact
21 lenses which have colours, designs or dyes with
22 particular characteristics incorporated into them.

23

24 The product of this invention can be designed to either
25 be clear for vision correction contact lenses or opaque
26 for cosmetic lenses or prosthetic lenses. The general
27 empirical rule for clear lenses is that the components
28 should be compatible in both the reaction mixture and in
29 the product. The well known solubility parameters
30 available may be used as a guide to materials that will
31 be compatible and produce clear lenses. Reaction
32 materials having large solubility parameter differences
33 but which provide a homogenous reaction mixture will be

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1 likely to produce opaque white material on
2 polymerisation. Such materials are desirable for the
3 simulation of bright white sclera for cosmetic or
4 prosthetic lenses. When reaction mixtures are changed
5 systematically within a series of identical reagents in
6 varying ratios, often both clear and opaque formulations
7 are formed from particular ranges of compositions made
8 from the same stock of starting materials.

9
10 It is worth noting that in many cases clear lenses occur
11 mainly when using aromatic amines and opaque when using
12 aliphatic amines, although this is not necessarily always
13 the case.

14

15 Examples

16

17 1. POLYMERS PREPARED BY USING THE ALIPHATIC AMINE
18 ETHYLENEDIAMINE (EDA) AND ALIPHATIC ISOCYANATE
19 DICYCLOHEXYLMETHANE-4,4'-DIISOCYANATE (DesmodurW). 1,2,6-
20 HEXANE TRIOL (HT) WAS ALSO USED. THE POLY(ETHYLENE
21 GLYCOL) (PEG) HAD A MEASURED NUMBER AVERAGE MOLECULAR
22 WEIGHT OF 3130 AND THE POLY(PROPYLENE GLYCOL) PPG A VALUE
23 OF 425.

24

25 The following compositions were prepared where the
26 symbols carry the usual names.

27

28 (a) PUU3130CX (0.5HT) (0.5EDA)

29

	<u>mol</u>	<u>intended wt</u>	<u>actual wt</u>
		<u>used (g)</u>	<u>used (g)</u>
32 PEG 3130	(1)	5.00	5.00
33 PPG 425	(15)	10.1837	10.188

1	HT	(0.5)	0.1071	0.1071
2	EDA	(0.5)	0.048g	0.050
3	DesmodurW	(18.11)	7.5950g	7.595
4	FeCl ₃	0.02 wt%	4.58mg	4mg

5

6 Procedure

7

8 The following method of preparation was used for all of
9 the examples that follow. All of the reaction components
10 were either dry as used or else they were dried (i.e.
11 the PEO AND PPG) using a "Rotavap" rotating heated vacuum
12 drier. The dry PEG , PPG and HT were placed in a beaker
13 and heated to 95C and mixed thoroughly with the aid of a
14 glass rod. The anhydrous ferric chloride catalyst was then
15 blended in small increments at a time with stirring
16 ensuring that each small addition was dissolved before
17 the next was added. When an amine was used it was added
18 and blended in a similar fashion. Finally the DesmodurW
19 diisocyanate was added as rapidly as possible with
20 stirring and the reaction allowed to proceed at 95C.

21

22 Cured for 20 hours at 95°C. The product was solid at room
23 temperature and thermoplastic at elevated temperatures.
24 It formed contact lenses, by the usual method of pressing
25 between polypropylene moulds, which were readily
26 demoulded when cold.

27

28 The lens was initially clear but became slightly hazy in
29 water.

30

31 The polymer swelled to high degree in tetrahydrofuran but
32 would not dissolve.

33

1 (b) PUU3130DX (0.5HT (0.5EDA)

2		<u>mol</u>	<u>intended wt.</u>	<u>actual wt</u>
3			<u>used (g)</u>	<u>used (g)</u>
4	PEG 3130	(1)	5.00	5.124
5	PPG 425	(20)	13.5782	13.580
6	HT	(0.5)	0.10717	0.1071
7	EDA	(0.5)	0.0480	0.059
8	DesmodurW	(23.3625)	9.7965	9.796
9	FeCl ₃	0.02 wt%	5.7mg	6mg

10

11 Procedure

12

13 Synthesised in the manner presented above. The product
14 was a soft solid which was thermoplastic. It was a
15 suitable material for further modification by reaction
16 with amine or hydroxyl-containing modifiers as is
17 illustrated for a related composition in the following
18 example in which the proportion of isocyanate-containing
19 component DesmodurW is increased.

20

21 The compression method afforded lenses very easily from
22 this product without further reaction but the product was
23 very sticky and did not demould in dry state. The lens
24 with mould was immersed in water over weekend after which
25 time the lens had swollen off it's support. It was
26 soluble in THF.

27

28

29 2. A STAGE1 POLYMER WITH EXCESS OF ALIPHATIC ISOCYANATE
30 AND A LINEAR ALIPHATIC AMINE (0.75 EDA)

31

32 PUU3130CX(0.5HT) (0.75 EDA) with excess of DesmodurW

33

	<u>mol</u>	<u>intended wt.</u>	<u>actual wt.</u>
		<u>Used (g)</u>	<u>used (g)</u>
PEG 3130	(1)	5.00	5.00
PPG 425	(15)	10.1837	10.188
HT	(0.5)	0.1071	0.1071
EDA	(0.75)	0.071	0.072
DesmodurW	(44.0)	18.450	18.375
FeCl ₃	0.02 wt%	4.58mg	5mg

Procedure

The usual method. The product solidified on cooling but melts when hot.

This product produced lens-shape by the usual method. The product was immersed in water when it fragmented. White sections of polymer were obtained in the lens mould. This material was soluble in methanol and precipitated when a little water were added. The product was also soluble in tetrahydrofuran. It is not suitable for moulding into lenses but is used here to exemplify the ready formation of end-capped modified thermoplastic polymers using the following end group modifiers by:

2.a Reaction with benzylamine in the absence of solvent.

2.b Reaction with butylamine in the absence of solvent

2.c Reaction with dibutylamine in the absence of solvent

Those expert in the synthesis of polymers would readily see how to extend this procedure to many other simple amine or hydroxyl-containing molecules and to end-capping

1 with many amine and hydroxyl ended low-molecular weight
2 polymers.

3

4 2.a Reaction with Benzylamine

5

6 Wt of the prepolymer with excess isocyanate = 4.275g

7 Wt of the benzylamine = 1.00g

8

9 Procedure

10

11 Both materials were mixed and allowed to react at 95°C for
12 half an hour. The materials were in a round bottom flask
13 that was rotated using a rotary evaporator while immersed
14 in an oil bath at 95°C.

15

16 The product was thermoplastic and fluid and could be
17 readily moulded into a lens that appeared optically
18 transparent though it was fragile and broke when attempts
19 were made to detach it from the mould.

20

21 2.b Reaction with Butylamine

22

23 Weight of the prepolymer = 4.278g

24 Weight of the butylamine = 1.380g

25

26 Procedure

27

28 The reaction was carried out in a beaker placed in an
29 oven at 95°C with stirring manually, using a glass rod.
30 The polymerising mixture was cured for 2 hours at 95°C.
31 The product was a brittle, hard, thermoplastic which
32 forms a clear lens.

33

1 2.c Reaction with Dibutylamine

2

3 Weight of the stagel polymer = 4.275g

4 Weight of the benzylamine = 1.380g

5

6 The procedure used was the same as described in (2.b).

7

8 The product was a sticky, thermoplastic which can be
9 moulded into a lens easily but is physically rather weak
10 after immersion in water.

11

12 3. PREPOLYMER WITH EXCESS OF OH GROUPS CONTAINING EXCESS
13 HYDROXYL AND UREA UNITS FORMED USING AN AROMATIC AMINE
14 DIPHENYLMETHANE-4,4'-DIISOCYANATE (DPDA).

15

16 PUU3130CX(0.5HT) with excess of alcohol groups

17

18		<u>mol</u>	<u>intended wt</u>	<u>actual wt</u>
19			<u>used (g)</u>	<u>used (g)</u>
20	PEG 3130	(1)	10.00 g	10.01
21	PPG 425	(15)	20.3674	20.376
22	HT	(0.5)	0.2143	0.214
23	EDA	(0.5)	0.3167	0.317
24	DPDA	(10.25)	8.5962	8.63 g
25	FeCl ₃	0.02 wt%	7.96 mg	8.0 mg

26

27 The prepolymer was prepared as above and remained liquid
28 after 5 hours of reaction at 95°C. The mixture could not
29 be gelled and demonstrates the ability of compositions
30 having a suitable excess of one of the reacting groups to
31 provide a stagel polymer without the possibility of
32 gelling in the reaction vessel. On cooling the material
33 solidifies but melts again when heated. It forms a

1 useful basis for either end-capping with desired
2 materials or for preparing reactive mixtures which can be
3 formed into lens shapes and subsequently crosslinked by
4 heating. Because of its fast rate of reaction the
5 aliphatic diisocyanate DPDA is a very suitable
6 crosslinking agent.

7

8 This prepolymer was used for the following curing
9 reaction:

10

11 The Prepolymer and Desmodur W

12

13 Weight of the stage 1 polymer with excess of alcoholic
14 groups =10.0 g

15 DesmodurW added to the same beaker =1.467 g

16

17 Mixed well. The resulting very fluid material was poured
18 into a polypropylene tube and cured for 4 hours at 95°C.
19 The polymer gelled sometime within 2 hours and on cooling
20 provided a strong crosslinked product. This would clearly
21 have been able to be moulded and formed into crosslinked
22 lenses before the second stage curing.

23

24 Incorporation of antioxidant butylated hydroxyl anisole

25 (BHA) and using diphenylmethane-4,4'-diamine (DPDA)

26 PUU5950 BX (0.75 HT)

27

	<u>mol</u>	<u>intended wt.</u>	<u>Actual wt</u>
		<u>used (g)</u>	<u>used (g)</u>
30 PEG 5950	(1)	10	10.00
31 HT	(0.75)	0.1691	0.169
32 PPG 425	(10)	7.1428	7.147
33 DesmodurW	(13.2562)	5.8483	8.63 g

1	BHA	(0.03% by	3 mg	3 mg
2		wt of PEG)		
3	DPDA	(0.5)	0.1666	0.166
4	FeCl ₃	0.02 wt%	4.66 mg	4.0 mg

5

6 When BHA added to the reaction there was a very slight
 7 darkening in the colour. change in colour. The reaction
 8 product was fluid and could be moulded into clear contact
 9 lenses.

10

Procedure

12

13 HT and PPG, FeCl₃ and DPDA, BHA and D were mixed in this
 14 order and allowed to cure in polypropylene test-tube.

15

16		<u>mol</u>	<u>intended wt</u>	<u>actual wt</u>
17			<u>used (g)</u>	<u>used (g)</u>
18				
19	PEG 5950	(1)	10	10.02
20	HT	(0.75)	0.1691	0.171
21	PPG 425	(10)	7.1428	7.147
22	DesmodurW	(13.2562)	5.8483	8.63 g
23	BHA	.3% by wt.	0.3000 mg	0.305 mg
24		of PEG)		
25	DPDA	(0.5)	0.1666	0.166
26	FeCl ₃	0.02 wt%	4.66 mg	6.0 mg

27

28 In the case of the very high 3% level of BHA the reaction
 29 became immediately very dark but returned to slightly
 30 darker yellow than expected without BHA when PEG was
 31 added and mixed. No other visual effect was observed and
 32 the product set solid when cold and became fluid and

1 mouldable when hot when it could be moulded readily into
2 transparent lenses

3

4 These results show that the antioxidant BHA can be
5 incorporated into the stagel reaction.

6

7

8 **4. THERMOPLASTIC HYDROGELS SUITABLE FOR USE IN CLEAR**
9 **VISION CORRECTION CONTACT LENSES.**

10

11 Thermo plastic hydrogelcompositions were made from
12 poly(ethylene glycol), poly(propylene glycol), 1,2,6-
13 hexane triol, dicyclohexylmethane-4,4'-diisocyanate and
14 diphenylmethane-4,4'-diamine(DPDA). The overall
15 composition has a functionality of >2.

16 Three batches of poly(urethane urea) denoted PUU polymers
17 coded PUU 5950 BX (0.5 HT), PUU 5950 BX (0.6 HT), and PUU
18 5950 BX (0.75 HT) were prepared by a single step bulk
19 polymerisation method described below. The molar
20 compositions and the weight compositions are given in the
21 next two tables below.

22

23 **Chemical compositions PUU polymers**

Polymer unit denoted as	SOFT BLOCKS		HARD BLOCKS		TRIOL
	PEG	PPG 425	DPDA	Desmodur W	HT
	moles	(moles)	(moles	(moles)	(mole s)
PUU5950 BX (0.5HT) Batch 1,2,3	1	10	0.5	12.8625	0.5
PUU5950 BX (0.6HT) Batch 1,2,3	1	10	0.5	13.02	0.6

PUU5950 BX (0.75HT)	1	10	0.5	13.2562	0.75
Batch 1,2,3					

1
2 Ferric chloride catalyst was used as 0.02 wt% of the
3 reactants
4 DesmodurW was used as 5 mol% in excess of stoichiometric
5 quantity
6 The appropriate quantities of hexane triol (HT) and
7 dehydrated PPG 425 weighed into a beaker to which the
8 calculated quantity of ferric chloride catalyst was
9 added. The beaker was then placed in the oven at 95 C.
10 Within ~15 minutes the catalyst dissolved assisted by
11 occasional stirring. The DPDA was then added, mixed and
12 left in the oven. Once the DPDA had dissolved the
13 dehydrated molten PEG was added, mixed thoroughly and
14 left in the oven for few minutes. Finally, the required
15 amount of Desmodur W (dicyclohexylmethane-4,4'-
16 diisocyanate) was directly weighed into the beaker
17 containing the other reactants, mixed and left in the
18 oven with occasional stirring for 15 minutes. This was
19 then poured into preheated polypropylene moulds and
20 placed in the oven at 95 deg C to cure over 22 hours.
21 After this period the oven was switched off, the product
22 was allowed to cool and readily demoulded after quenching
23 in liquid nitrogen.

24 Weights of reactants used

25

Polymer denoted as	SOFT BLOCK		HARD BLOCK		Triol
	PEG (g)	PPG 425 (g)	DPDA (g)	Desmodur W (g)	
PUU5950BX (0.5HT)	10	7.1428	0.166	5.6746	0.1127

Batch1,2,3			6		
PUU5950BX (0.6HT)	10	7.1428	0.166	5.7441	0.1353
Batch1,2,3			6		
PUU5950 BX (0.75HT)	10	7.1428	0.166	5.8483	0.1691
Batch1,2,3			6		

1

2 Ferric chloride was used as 0.02 wt% of the reactants

3 DesmodurW was used as 5 mol% in excess of stoichiometric
4 quantity5 Actual amounts of the materials used were kept close to
6 the calculated values

7

8 **Swelling test.**

9

10 Slices from polymer billets were cut and three slices of

11 ~~essentially identical thickness were allowed to swell to~~
 12 equilibrium in water at ambient temperature. The swelling
 13 (%) calculated by the equation: % swelling = Weight of
 14 the swollen slice - weight of the dry slice/weight of the
 15 swollen slice. The three test results were averaged.

16

17 **Test of thermoplasticity.**

18

19 A small disk of the thermoplastic hydrogel was placed
 20 between two polypropylene moulds which when compressed
 21 formed a prescription contact lens shape between their
 22 faces. The disk was placed into the female section and
 23 the male half of the mould was placed on top. After 10
 24 minutes heating at 95C the ability of the test
 25 thermoplastic hydrogel composition to flow and form a
 26 contact lens when cooled to room temperature was
 27 evaluated under the pressure between the thumb and
 28 forefinger. The mould was cooled and the solid moulded

- 1 contact lens removed using forceps and then made
 2 available for testing.
 3
 4 Average swelling of PUU polymers in water at ambient
 5 temperature.
 6

Polymer composition	Swelling data (pph)	Swelling data (%)	Average Swelling (%)
PUU5950BX (0.5HT) Batch 1	253.6	72	
PUU5950BX (0.5HT) Batch 2	253.7	72	
PUU5950BX (0.5HT) Batch 3	244.8	71	72

7

PUU5950BX (0.6HT) Batch 1	246.6	71	
PUU5950BX (0.6HT) Batch 2	229.9	70	
PUU5950BX (0.6HT) Batch 3	279.7	74	71

8

PUU5950BX (0.75HT) Batch 1	224.5	69	
PUU5950BX (0.75HT) Batch 2	239.3	70	
PUU5950BX (0.75HT) Batch 3	222.7	69	69

9

10 Swelling test results

- 11
 12 The results from the swelling tests in water at ambient
 13 temperature are summarised in Table 3. Only a small
 14 variation in the swelling values was seen in the polymers

1 that contained HT (see Table 3) in spite of the
2 significant change in the amount of the triol used. The
3 visual appearance of the swollen polymers also varied. It
4 was observed that the PUU 5950 BX (0.5 HT) polymer
5 occasionally afforded "frostiness" possibly due to micro
6 stress cracking in the water- swollen state. Polymer PUU
7 5950 BX (0.6 HT) with slightly increased HT from 0.5
8 molar to 0.6 molar showed the effect in an occasional
9 batch. However such "frostiness" in PUU 5950 BX(0.75HT)
10 was not observed at all. The lenses produced were
11 transparent and the obtained degree of swelling of 69% is
12 a very useful figure for contact lenses.

13

14 Some selected results from GPC analysis of PUU polymers

15

Polymer	M_n	M_w	M_w/M_n
PUU5950BX (0.5HT) Batch 1	6.603×10^3	1.674×10^4	2.535 ± 0.044
PUU5950BX (0.5HT) Batch 2	6.399×10^3	1.456×10^4	2.275 ± 0.038
PUU5950BX (0.5HT) Batch 3	6.049×10^3	1.349×10^4	2.231 ± 0.059

16

17

18 The following conclusions can be drawn from the above

19

20 All polymer compositions investigated were
21 thermoplastic and afforded contact lenses when
22 subjected to the compression technique.

23

1 ▪ The chemical structure of all the polymer
2 compositions were shown to be similar by the FTIR
3 analysis and reproducible within three batches of a
4 given polymer composition.

5
6 ▪ GPC analysis Table 4 confirmed good reproducibility
7 among three batches of a given polymer composition.
8 The polydispersity values of all the polymers were
9 from 2.2-2.6 . These values are quite broad but
10 consistent with that to be expected from a step-
11 growth polymerisation. The M_w and M_n values within
12 three batches of a given polymer composition were
13 quite similar - a desired result and indicates a
14 good reproducibility.

15
16 ▪ FTIR analysis clearly indicated that free primary
17 amine of DPDA after polymerisation has disappeared
18 and been converted to secondary amine to form a
19 urethane/urea group of the polymer structure.

20

21 **5. PREPARATION OF THERMOPLASTIC HYDROGELS FROM A**
22 **POLYURETHANE WITHOUT THE USE OF A DIAMINE AS A COMPONENT**
23 **OF THE STAGE 1 COPOLYMER**

24

25 The polymers were made according to a closely similar to
26 the procedure described previously.above. The reactants
27 were poly(ethylene glycol) described by the supplier as
28 PEG6000 and meaning a PEG having a number average
29 molecular weight close to 6000. 1,2,6-hexanetriol, and
30 dicyclohexylmethane-4,4'-diisocyanate (DesmodurW) and
31 using anhydrous ferric chloride (0.2mg per g. of
32 reactants) as the catalyst. The molar proportions used
33 are given in Table 4 below. Other compositions made

1 nearer to stoichiometry of the hydroxyl and isocyanate
2 groups crosslinked during the curing reaction so at
3 complete reaction could not provide thermoplastic
4 hydrogels. They would have done so if the reactions had
5 been terminated prior to complete reaction.

6

Preparation number	PEG6000	1,2,6- HEXANETRIOL	Desmodur W
1	1 MOLE	1 MOLE	3.75
2	1 MOLE	1 MOLE	5.0

7

8 After four hours cure at 90C the products were cooled
9 demoulded and stored in sealed bags away from air and
10 light. A few of the samples were converted into thin
11 slices and sample slices were evaluated for their
12 ability to thermoform in a "Rosslyn" heat press. At
13 115C the slices became very fluid and could be pressed
14 into thin films. These became solid at 110C and formed
15 solid pliable hydrogel films.

16

17 Cut film samples were allowed to swell in water to
18 equilibrium when they became clear transparent gels.
19 They were insoluble in water but swelled to a high
20 degree as given in the table below.

21

Sample	Dry weight of slice in g.	Swollen weight of slice	% equivalent of isocyanate in the preparation
1	.730	3.845	1.5
2	.223	2.282	2.0

1
2 Sample 1 was completely soluble in methanol demonstrating
3 that it was not a crosslinked gel before contact with
4 water when the residual isocyanate groups would have been
5 converted to urea crosslinks.

6
7 It can be seen that the embodiments disclosed are both or
8 merely exemplary of the present invention, which may be
9 embodied in many different forms. Therefore, details
10 disclosed herein are not to be interpreted as limiting,
11 but merely as a basis for the claims and for teaching one
12 skilled in art as to the various uses of the present
13 invention in any appropriate matter. In particular, it
14 should be noted that a wide variety of changes can be
15 made in this process.

16
17 For example, pre-polymers with excess OH can be capped
18 with a mono-isocyanate ended aromatic or aliphatic
19 molecule or with a reaction product of a mono-amine with
20 di or higher isocyanate. The low molecular weight amine
21 could be replaced with a low molecular weight polymeric
22 amine, such as low M_n primary and secondary amine ended
23 nylon polyamide) or polypropylene oxide, poly(butanediol)
24 or low molecular weight polymers producing glassy domains
25 such as end-capped polystyrenes or amine end-capped
26 hydrophobic and crystalline domain forms such as
27 poly(ethylene) units. The reaction can be between such
28 amine ended PEGs (poly(ethylene glycols)) and PPGs
29 (poly(propylene glycols)) and di or higher amines and di
30 or higher isocyanates, but done in solvents to allow
31 suitable reduced viscosity to be obtained. Also, to slow
32 down the amine reaction, the amine can be added at the

1 outset as the carbonate version of amine carbonate,
2 resulting from the reaction of amine and carbon dioxide.

3

4 Also, stage one hydroxlic excess polymers could be
5 reacted with a phase separating polymer end capped with
6 an anhydride group.

7

8 Finally, it should be noted that this end capping process
9 could be applied to a wide variety of polymers, such as
10 polyesters, nylons, polyurethanes, polyureas, polyethers,
11 polyolefins, polyvinyls and poly(meth)acrylates.

1 Claims

2

3 1. A method of producing thermoplastic hydrogels for use
4 in producing contact lenses, comprising the step of
5 reacting one or more from the list;

6 polyethylene oxide,

7 polyol,

8 polyamine,

9 with a polyisocyanate and a polyfunctional amine or
10 polyalcohol.

11

12 2. A method of producing thermoplastic hydrogels for use
13 in producing contact lenses, comprising the step of
14 reacting one or more from the list

15 polyethylene oxide

16 polyol

17 polyamine

18 and a polyisocyanate that is prepared using a range of
19 NCO:OH or NCO:NH₂ ratios.

20

21 3. A method of producing thermoplastic hydrogels as in
22 Claims 1 or 2 wherein the polyol is polyethylene
23 glycol.

24

25 4. A method of producing thermoplastic hydrogels as in any
26 of the previous Claims wherein the method also
27 comprises the step of end capping unreacted groups with
28 a unit capable of producing hydrogen bonding, π
29 bonding, ionic bonding, hydrophobic bonding and/or
30 phase separation or forming a glassy or crystalline
31 phase separated domain.

32

- 1 5. A method of producing thermoplastic hydrogels as in
2 Claims 1 - 3 wherein the method also comprises the step
3 of end capping unreacted groups with a unit from a list
4 of:
5 Mono-functional amine
6 Mono-functional isocyanate
7 Mono-functional anhydride
8 Mono-functional acid
9 A cyclic diacid anhydride
10 Mono-functional alcohol
11
- 12 6. A method of producing thermoplastic hydrogels as in any
13 of the previous Claims wherein a biodegradable unit may
14 be incorporated.
15
- 16 7. A method of producing thermoplastic hydrogels as in
17 Claim 6 wherein biodegradable unit may be
18 polycaprolactone, poly (lactic acid), poly(glycolic)
19 acid or poly(hydroxybutyric)acid, amine or hydroxyl
20 ended poly(amino) acids (protein or peptide analogues).
21
- 22 8. A method of producing thermoplastic hydrogels as in any
23 of the previous Claims wherein the ratios of the
24 components are selected such that, at complete
25 reaction, the product does not form a macrogel.
26
- 27 9. A method of producing thermoplastic hydrogels as in any
28 of the previous Claims wherein the reaction is prepared
29 using a range of NCO:OH or NCO:NH₂ ratios from 2:1 to
30 1:2.
31
- 32 10. A method of producing thermoplastic hydrogels as in
33 any of the previous Claims wherein where both OH and

1 NH₂ groups are used within the single reaction, a range
2 of NCO:(OH+NH₂) ratios of 2:1 to 1:2.

3

4 11. A method of producing thermoplastic hydrogels as in
5 any of the previous Claims wherein the first step
6 reaction is prepared using NCO:OH or NCO:NH₂ ratios of
7 2.0:1 to 1:1.8 and 1.8:1 to 1:1.8.

8

9 12. A method of producing thermoplastic hydrogels as in
10 any of the previous Claims wherein the range of ratios
11 used may be extended by the addition of monofunctional
12 amines, alcohols or cyanates.

13

14 13. A method of producing thermoplastic hydrogels as in
15 any of the previous Claims wherein a macrogel is
16 prevented from forming by stopping the reaction before
17 completion.

18

19 14. A method of producing thermoplastic hydrogels as in
20 Claim 13 wherein the reaction is stopped by the
21 addition of a monoamine, an amine terminated polymer, a
22 mono-alcohol or an alcohol terminated polymer.

23

24 15. A method of producing thermoplastic hydrogels as in
25 Claim 14 wherein the monoamine, mono-alcohol, amine
26 terminated polymer or alcohol terminated polymer is
27 added when the reaction is partially complete.

28

29 16. A method of producing thermoplastic hydrogels as in
30 Claims 1-12 wherein an amine or alcohol is admixed at
31 the outset thus removing the possibility of gelation.

32

- 1 17. A method of producing thermoplastic hydrogels as in
2 Claim 16 wherein the amine is added in the form of
3 amine carbonate.
4
- 5 18. A method of producing thermoplastic hydrogels as any
6 of the previous Claims wherein products with NCO end
7 groups are subjected to a final curing by immersion in
8 liquid water or steam after moulding.
9
- 10 19. A method of producing thermoplastic hydrogels as in
11 any of the previous Claims wherein, after the initial
12 reaction, a second stage occurs, and in the second
13 stage the unreacted groups are capped with an amine.
14
- 15 20. A method of producing thermoplastic hydrogels as in
16 Claim 19 wherein unreacted NCO groups are endcapped.
17
- 18 21. A method of producing thermoplastic hydrogels as in
19 Claim 19 wherein unreacted OH groups are endcapped.
20
- 21 22. A method of producing thermoplastic hydrogels as in
22 Claims 19 and 20 wherein terminal NCO groups are
23 converted into a strongly hydrogen bonding urea group.
24
- 25 23. A method of producing thermoplastic hydrogels as in
26 Claims 19-22 wherein the unreacted groups are capped
27 with an aliphatic amine.
28
- 29 24. A method of producing thermoplastic hydrogels as in
30 Claim 23 wherein the amine group is attached to a long
31 linear or branched alkyl group or to an aryl- or
32 aralkyl-amine.
33

1 25. A method of producing thermoplastic hydrogels as in
2 Claim 23 wherein the amine group is attached to
3 polymers or low molecular weight pre-polymers.
4

5 26. A method of producing thermoplastic hydrogels as in
6 Claims 19 and 21 wherein, excess OH groups are capped
7 with one or more molecules from the list of;
8 mono-isocyanate ended aromatic molecules,
9 mono-acid anhydride ended aromatic molecules,
10 mono-isocyanate ended aliphatic molecules,
11 mono-acid anhydride ended aliphatic molecules
12 reaction product of a monoamine with a di(or higher)
13 isocyanate.
14

15 27. A method of producing thermoplastic hydrogels as in
16 Claims 19-26 wherein the groups used in the endcapping
17 process allow the polymers to interact with physical or
18 chemical cross-linking.
19

20 28. A thermoplastic hydrogel for use in producing
21 contact lenses, prosthetic lenses or cosmetic lenses
22 produced by the methods described in Claims 1-27.
23

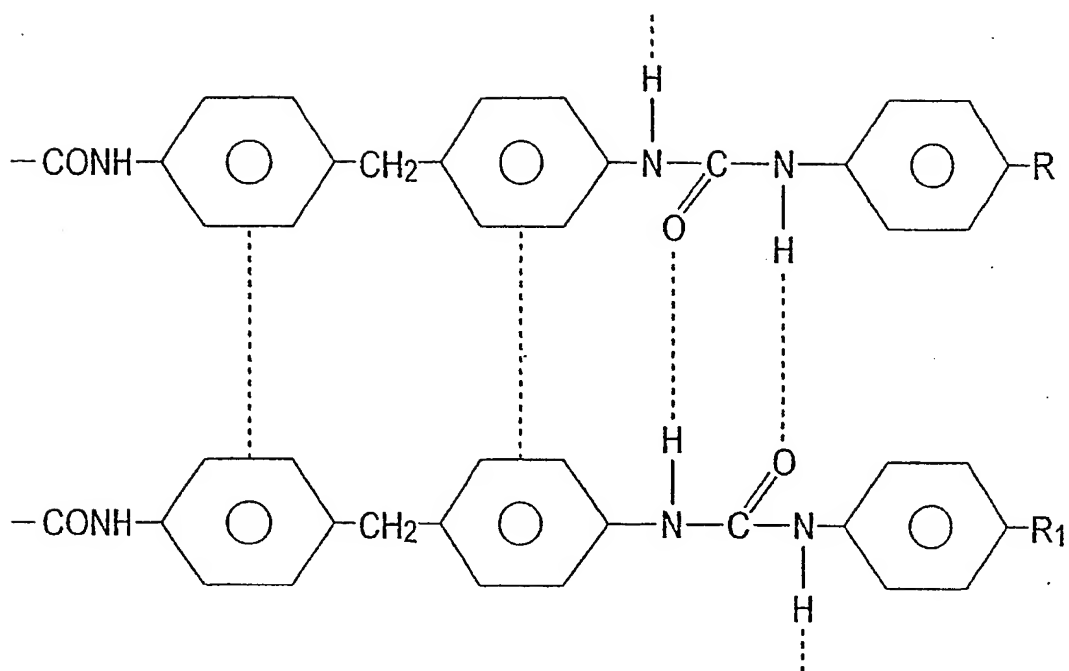
24 29. A thermoplastic hydrogel as in Claim 28 wherein the
25 hydrogel is completely polymerised under the specific
26 conditions that are being used.
27

28 30. A thermoplastic hydrogel as in Claims 28 and 29
29 wherein after polymerisation the hydrogel is heated.
30

31 31. A thermoplastic hydrogel as in Claims 28 and 29
32 wherein after polymerisation the hydrogel is immersed
33 in water liquid or vapour.

- 1
2 32. A thermoplastic hydrogel as in Claims 28 - 31
3 wherein the hydrogel may be pelletised, pressed,
4 extruded or heat, pressure, injection or compression
5 moulded.
6
- 7 33. A thermoplastic hydrogel as in Claims 28 - 32
8 wherein the end product incorporates an antioxidant
9 containing two or more hydroxyl groups.
10
- 11 34. A thermoplastic hydrogel as in Claim 33 wherein the
12 antioxidant may be internal or external.
13
- 14 35. A thermoplastic hydrogel as in Claims 33 and 34
15 wherein the antioxidant is ascorbic acid.
16
- 17 36. A thermoplastic hydrogel as in Claims 33 and 34
18 wherein the antioxidant is 2,6-ditertiarybutyl-4-
19 hydroxanisole.
20
- 21 37. A thermoplastic hydrogel as in Claims 28 - 36
22 wherein the hydrogel develops opacity when swollen in
23 water.
24
- 25 38. A thermoplastic hydrogel as in Claims 28 - 37
26 wherein the hydrogel incorporates dye(s).
27
- 28 39. A thermoplastic hydrogel as in Claims 28 - 38
29 wherein the hydrogel incorporates pigment.
30
- 31 40. A contact lens, prosthetic lens or cosmetic lens
32 produced from the hydrogel of Claims 28-39.

1/1

**FIG. 1**

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 03/03802

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C08G18/10 C08G18/66 G02B1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08G G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	FR 2 674 529 A (ESSILOR) 2 October 1992 (1992-10-02) page 1, line 4 - page 2, line 21; claims 1,6	1,7



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International

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